

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

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NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT AND
THE WRITTEN OPINION OF THE INTERNATIONAL
SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

Applicant's or agent's file reference 5941-65-PUS-CIP-PCT	Date of mailing (day/month/year) 06 FEB 2009
International application No. PCT/US 08/70930	International filing date (day/month/year) 23 July 2008 (23.07.2008)
Applicant THE REGENTS OF THE UNIVERSITY OF COLORADO	

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

When? The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.

Where? Directly to the International Bureau of WIPO, 34 chemin des Colombettes
1211 Geneva 20, Switzerland, Facsimile No.: +41 22 338 8270

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.

3. ☐ **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Reminders**

Shortly after the expiration of **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase **until 30 months** from the priority date (in some Offices even later); otherwise, the applicant must, **within 20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: <p style="text-align: center;">Lee W. Young</p> PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774
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PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 5941-65-PUS-CIP-PCT	<div style="display: flex; justify-content: space-between;"> <div> FOR FURTHER ACTION </div> <div> see Form PCT/ISA/220 as well as, where applicable, item 5 below. </div> </div>	
International application No. PCT/US 08/70930	International filing date (<i>day/month/year</i>) 23 July 2008 (23.07.2008)	(Earliest) Priority Date (<i>day/month/year</i>) 23 July 2007 (23.07.2007)
Applicant THE REGENTS OF THE UNIVERSITY OF COLORADO		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 4 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of:

- ☒ the international application in the language in which it was filed.
☐ a translation of the international application into _____ which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

b. ☐ This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6*bis*(a)).

c. ☒ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☒ **Certain claims were found unsearchable** (see Box No. II).

3. ☒ **Unity of invention is lacking** (see Box No. III).

4. With regard to the **title**,

- ☒ the text is approved as submitted by the applicant.
☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

- ☒ the text is approved as submitted by the applicant.
☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings**,

a. the figure of the drawings to be published with the abstract is Figure No. 1

- ☒ as suggested by the applicant.
☐ as selected by this Authority, because the applicant failed to suggest a figure.
☐ as selected by this Authority, because this figure better characterizes the invention.

b. ☐ none of the figures is to be published with the abstract.

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Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item I.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of:

a. type of material

☒

a sequence listing

☐

table(s) related to the sequence listing

b. format of material

☐

on paper

☒

in electronic form

c. time of filing/furnishing

☐

contained in the international application as filed

☒

filed together with the international application in electronic form

☐

furnished subsequently to this Authority for the purposes of search

2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

INTERNATIONAL SEARCH REPORT

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Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☒ Claims Nos.: 13-22 and 35-39
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Invention 1: claims 1, 2, 8-12, 23-24, 30-34, 40-42, 48-49, 55-65, 70, 75-76 and 81-82, limited to the gene E-cadherin and SEQ ID NO: 3. Please note that there is an un-numbered claim between claims 70 and 71. This un-numbered claim also falls under the grouping of Invention 1.
Invention 2: claims 1, 3, 8-12, 23, 25, 30-34, 40-41, 45, 48, 50, 55-64, 66, 70, 71, 75, 77, 81 and 83, limited to the gene RAB25 and SEQ ID NO: 83.
Invention 3: claims 1, 4, 8-12, 23, 26, 30-34, 40-41, 46, 48, 51, 55-64, 67, 70, 72, 75, 78, 81 and 84, limited to the gene integrin beta 6 (ITGB6) and SEQ ID NO: 137.
Invention 4: claims 1, 4, 8-12, 23, 26, 30-34, 40-41, 46, 48, 51, 55-64, 68, 70, 73, 75, 79, 81 and 85, limited to the gene integrin beta 6 (ITGB6) and SEQ ID NO: 52.
Invention 5: claims 1, 5, 8-12, 23, 27, 30-34, 40-41, 47-48, 52, 55-64, 69, 70, 74-75, 80-81 and 86, limited to the gene vimentin and SEQ ID NO: 195.
Invention 6: claims 1, 6, 8-12, 23, 28, 30-34, 40-41, 43, 48, 53, 55-64, 70, 75, 81 and 87, limited to the gene ZEB1 and SEQ ID NO: 196.
Invention 7: claims 1, 7-12, 23, 29-34, 40-41, 44, 48, 54-64, 70, 75, 81 and 88, limited to the gene SIP1 and SEQ ID NO: 197.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: claims 1, 2, 8-12, 23-24, 30-34, 40-42, 48-49, 55-63, 64a, 64b, 65a, 65b, 70, 75-76 and 81-82, limited to the gene E-cadherin and SEQ ID NO: 3.

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 08/70930

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - C12Q 1/68, C40B 30/04, A61P 35/00 (2008.04)

USPC - 435/6, 435/7.23, 506/9

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

USPC -435/6, 435/7.23, 506/9

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

PubWEST(USPT,PGPB,EPAB,JPAB); PubMed; Google Scholar

Search Terms Used: sensitive, resist, cetuximab, panitumumab,nimotuzumab,matuzumab, epithelial , cancer,tumor,E cadherin,EGFR , antibody

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 2006/0211060 A1 (HALEY et al.) 21 September 2006 (21.09.2006)entire document, especially para [0016],[0018], [0020],[0025][0039],[0133],[0190]	1,2, 8, 9, 23, 24, 30, 31, 40-42, 48, 49, 61, 62 10-12, 32-34, 55-60, 63, 64a, 64b, 65a, 65b, 70, 75-76, 81-82
Y	US 2007/0020261 A1 (SLIWKOWSKI et al.) 25 January 2007 (25.01.2007) entire document, especially para [0044], [0084],[0087], [0201]	10, 12, 32, 34, 55-60, 63, 65a
Y	ALLAN, Nimotuzumab: Evidence of Clinical Benefit Without Rash, The Oncologist, May 2005, Vol 10, No 9, pp 760-761	11, 33, 64a
Y	US 2002/0045591 A1 (GEIGER et al.) 18 April 2002 (18.04.2002) entire document, especially para [0101], SEQ ID NO: 47	64b, 65b, 70, 75, 76, 81, 82, 89

☐ Further documents are listed in the continuation of Box C.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T"

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X"

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&"

document member of the same patent family

Date of the actual completion of the international search

31 December 2008 (31.12.2008)

Date of mailing of the international search report

06 FEB 2009

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents
P.O. Box 1450, Alexandria, Virginia 22313-1450

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Authorized officer:

Lee W. Young

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